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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 01E-0363]

Determination of Regulatory Review Period for Purposes of Patent Extension; MIFEPREX; Amendment

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; amendment.

SUMMARY: The Food and Drug Administration (FDA) is amending a previous determination of the regulatory review period for MIFEPREX that appeared in the FEDERAL REGISTER of January 25, 2002 (67 FR 3724). The agency is taking this action in response to received comments. FDA is publishing notice of that amendment as required by law.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.fda.gov/dockets/ecomments.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: In the FEDERAL REGISTER of January 25, 2002 (67 FR 3724), FDA published its determination of the regulatory review period for MIFEPREX. On June 10, 2002, Corcept Therapeutics, Inc., (Corcept) filed a request for revision of the regulatory review period. On July 2, 2002, the applicant filed a comment, disagreeing with Corcept's request and maintaining that FDA's initial determination was correct.

The basis of Corcept's request is that August 4, 1994, is not the correct date an investigational new drug application (IND) covering the approved drug product became effective. Corcept asserts that June 13, 1983, is the appropriate date. FDA has re-examined its records and has determined that Corcept is correct. The date an exemption under section 505 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355) became effective is June 13, 1983.

The agency, the applicant, and Corcept agree that the relevant IND is IND 22,047. All agree that IND 22,047 became effective in 1983.

The applicant's argument for keeping the initial determination is based on the claim that August 4, 1994, represents the date the IND first covered the "approved human drug product." While acknowledging that IND 22,047 became effective in 1983, the applicant observes that during the next several years the only studies conducted were studies of mifepristone alone, that is, not in conjunction with the

administration of other drugs. The 1994 date is when the applicant submitted an amendment to IND 22,047 to initiate studies of mifepristone when followed by the later administration of misoprostol. The final approved MIFEPREX labeling recommends that patients taking mifepristone take 400 micrograms of misoprostol 2 days after taking mifepristone unless a complete abortion has already been confirmed before that time. The applicant argues from these facts that the submission of the 1994 amendment represents the first time an IND for the "approved human drug product," as set forth in 21 CFR 60.22(a)(1), became effective.[1]

The investigational path of a new drug is rarely straightforward. From the time of the first submission of an IND to the time, usually years later, of final approval for marketing, the course of drug investigation goes up many blind alleys and frequently takes off in new directions. Rarely, if ever, is a drug approved under precisely the same conditions (i.e., indication(s), patient population(s), dosing regimen(s), duration of treatment, use in conjunction with other drugs, etc.) for which it is initially investigated. The decision to investigate MIFEPREX in conjunction with misoprostol under

[1] For purposes of part 60 (21 CFR part 60), "human drug product" is defined as "the active ingredient of a new drug or human biologic product (as those terms are used in the act and the Public Health Service Act), including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient." (See 21 CFR 60.3(b)(10).)

certain circumstances is typical of the kind of change that can occur in the investigation of a new drug.[2]

The applicant misperceives the nature of FDA's task in this kind of proceeding, one FDA has performed hundreds of times since 1984. A determination of the regulatory review period under 35 U.S.C. 156(g)(1)(B) is straightforward and largely ministerial in nature. Our role is not to probe a drug's investigational course and determine at what point in that course emerges the "approved human drug product." To do so would be to insert into a purely ministerial function an arbitrary element of uncertainty that would clearly subvert the purpose of the statute.[3]

The relevant IND became effective on June 13, 1983. That fact, upon which everyone agrees, is all that FDA need or should find in conducting the relevant portion of its regulatory review determination of MIFEPREX.[4]

Therefore, FDA has determined that the applicable regulatory review period for MIFEPREX is 6,318 days. Of this time, 4,662

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[2] The applicant tries to characterize MIFEPREX as mifepristone "in combination with another active ingredient" in an attempt to take advantage of portions of the definition of "human drug product" in 35 U.S.C. 156(f), that is, a human drug product means "the active ingredient of a new drug * * * as a single entity or in combination with another active ingredient." The applicant points to the definition of "combination product" at 21 CFR 3.2(e)(3) in this effort. A more useful description of a drug "in combination with another active ingredient" is found at 21 CFR 300.50 (two or more drugs combined in a single dosage form). MIFEPREX is not mifepristone "in combination with another active ingredient." MIFEPREX is single entity mifepristone.

[3] Indeed, using the kind of scrutiny recommended by the applicant, one could argue that the testing phase should be entirely disregarded for purposes of regulatory review period determinations because final labeling of any product, an essential element of an approved human drug product, is not established until well after the testing phase is complete.

[4] In our initial determination, we did not take into account the effect of 35 U.S.C. 156(g)(4)(C) and, instead, accepted as harmless the applicant's request for a later date.

days occurred during the testing phase of the regulatory review period, while 1,656 days occurred during the approval phase.

These periods of time were derived from the following dates, summarized from the January 25, 2002, notice and modified by this amendment:

1. The date an exemption under section 505 of the act (21 U.S.C. 355) became effective: June 13, 1983. The applicant claims August 3, 1994, as the date the IND became effective. However, for the reasons discussed previously, FDA has determined the IND effective date was June 13, 1983.

2. The date the application was initially submitted with respect to the human drug product under section 505 of the act: March 18, 1996. FDA has verified the applicant's claim that the new drug application (NDA) for MIFEPREX (NDA 20-687) was initially submitted on March 18, 1996.

3. The date the application was approved: September 28, 2000. FDA has verified the applicant's claim that NDA 20-687 was approved on September 28, 2000.

This determination of the regulatory review period establishes the maximum potential length of a patent extension. In its application for patent extension, the applicant seeks 1,825 days of patent term extension. However, the U.S. Patent

and Trademark Office applies several statutory limitations in its calculations of the actual period for patent extension.

Dated: October 16, 2002.

October 16, 2002.

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